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Letter to the Editor

Diagnosis of Melanoma Under Concomitant Natalizumab Therapy

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To the Editor: We have read with great interest the short report on natalizumab and melanoma from Bergamaschi and Montomoli published recently in this journal.¹ Natalizumab (Tysabri, Biogen Idec and Elan Pharmaceuticals) is a humanized monoclonal antibody against α_4 integrins used in the treatment of multiple sclerosis and Crohn's disease.² Mullen et al reported on two cases of melanoma in patients with multiple sclerosis receiving natalizumab.³ Their letter was criticized since case reports in general show limited interpretability in establishing cause-and-effect relationships³ and since controlled clinical trials and postmarketing surveillance studies did not indicate an increased risk of melanoma in patients receiving natalizumab.² However, melanoma is underreported to cancer registries as compared to other cancers due to its occurrence in the outpatient setting⁵ and therefore, postmarketing surveillance studies might also underestimate the true incidence of melanomas as side-effect of any drug therapy. We report here on a 41-year-old woman who had been treated with natalizumab (once per month i.v.) for 15 months for multiple sclerosis. The patient had no known history of melanoma but displayed many atypical moles for years that were regularly checked by a dermatologist. The family history was negative for melanomas and she did not expose herself to sunlight regularly. She noticed a rapidly growing mole on her upper arm. On evaluation it proved to be a superficial spreading melanoma in situ pTis (SSM-type) on the basis of a dysplastic nevus of a compound-type. The lesion was excised in total. Other moles were also removed but did not show any histological signs of melanoma. An eye examination with a special focus on the retina revealed no signs of ocular melanoma. The patient is now on regular follow-up with a dermatologist and showed no other transdifferentiation of the known nevi. She is still on natalizumab therapy.

The occurrence of melanoma in our patient was in close temporal relation to the administration of natalizumab and an alteration in a long-standing nevus. It should be taken into account that anti- α_4 - integrin antibodies suppress the immune system by inducing apoptosis in lymph-node T cells in an in vitro model⁶ which could explain the potential of melanoma cells to spread. The already published case reports together with the present case report should raise the awareness of this possible side effect of developing melanoma under natalizumab therapy. Medical doctors using natalizumab should consider regular dermatological check-ups for their patients until further data are available.

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